



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

72

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/773,446	02/09/2004	George Inana	GMR-0001	4156
7590 Margaret J. McLaren, Ph.D., Esq. 6500 SW 133rd Drive Miami, FL 33156		02/07/2007	EXAMINER JUEDES, AMY E	
			ART UNIT 1644	PAPER NUMBER
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		02/07/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)
	10/773,446	INANA ET AL.
	Examiner	Art Unit
	Amy E. Juedes, Ph.D.	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 07 November 2006.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1,2,4-17,53,57,58 and 60 is/are pending in the application.
 4a) Of the above claim(s) 14 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 1,2,4-13,15-17,53,57,58 and 60 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1644

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 11/7/06 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/7/06 has been entered.

Claims 1-2, 10-11, 13, 15-17, and 53 have been amended.

Claims 3 and 18-39 have been cancelled.

Claims 1-2, 4-17, 53, 57-58, and 60 are pending.

Claim 14 stands withdrawn from further consideration pursuant to 37 CFR 1.14209 as being drawn to a nonelected invention.

Claims 1-2, 4-13, 15-17, 53, 57-58, and 60 are under examination.

2. Upon reconsideration, and in view of Applicant's citation of specific support on pages 31, 40 and 41 of the specification, the rejection of the claims under 35 U.S.C. 112 first paragraph for new matter, as outline in section B) of the previous office action is withdrawn.

3. The rejection of the claims under 35 U.S.C. 102 is withdrawn. Specifically, Applicant's argument regarding MPEP 2131.02, and the selection of the claimed invention from the broad classes of unrelated diseases and diverse list of inhibitors of adverse proteases disclosed by the '440 publication is persuasive. Upon reconsideration, the classes of diseases and adverse proteases disclosed by the '440 publication are not sufficiently limited or well delineated to at once envisage selecting an inhibitor of MMP-14 to treat AMD, as is required by MPEP 2131.02.

4. The instant claims encompass methods comprising contacting with any agent that decreases the expression or activity of MT1-MMP. However, the instant claims are only being considered as they read on the elected group of agent (i.e. antibodies), until such time as the elected group is found to be allowable.

Art Unit: 1644

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 58 and 60 stand rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

As set forth previously, The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

D) The method wherein the antibody is administered by injection to the eye or subretinal space (Claims 58 and 60).

In the Preliminary Amendments, filed 8/11/05 and 8/19/05, Applicant indicates that support for the new limitations of Claim 1 can be found at pages 8 and 31 of the specification.

Regarding D), at pg. 53, the specification discloses delivery of a vector by intraocular injection. However, the disclosure does not recite administering an antibody. It is noted that all cites relating to administration of an antibody are found in specific examples and not in generic disclosures. Thus, Applicant has improperly attempted to claim specific limitations set forth only in specific examples of the more generic claims of the instant application.

Applicant's arguments filed 1/7/06 have been fully considered, but they are not persuasive.

Regarding injection into the eye, Applicant argues that the disclosure on page 40 that an anti-MT1-MMP antibody might be used in the eyes of patients with AMD provides adequate support for the instant claims.

However, the instant claims encompass treating any retinal or choroidal degenerative disease by administering an anti-MT1-MMP antibody into the eye. In contrast the specification discloses "using" said antibody to treat AMD. Treating AMD, as disclosed by the specification, has a much narrower scope than treating retinal or choroidal degenerative diseases.

Art Unit: 1644

Furthermore the generic disclosure of "using" an antibody in the eyes does not provide adequate support for injecting the antibodies into the eyes, as claimed. For example "using" the antibodies in the eyes might encompass topically applying the antibody to the eye, and has a much broader scope than injecting the antibody.

Applicant further argues that the disclosure on page 54 that an agent directed against MT1-MMP protein present in the outer retina, for example within the subretinal space, can provide a beneficial effect, provides adequate support for injection into the eye or subretinal space.

However, the cite on page 54 simply discloses that an agent that targets MT1-MMP, which is expressed in the outer retina or subretinal space may be effective for treatment. However, page 54 does not specifically disclose how the agent is to be administered, as recited in claims 58 and 60.

6. The following are new grounds of rejection.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 4-13, 15-17, 53, 57-58, and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are drawn to treating retinal or choroidal conditions by contacting with an antibody that decrease the expression of the MT1-MMP gene comprising the nucleotide sequence of SEQ ID NO: 15. It is unclear how an antibody specific for MT1-MMP would result in decreased gene expression.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

Art Unit: 1644

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-2, 4-13, 15-17, 53, 57-58, and 60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, there is insufficient written description to demonstrate that applicant was in possession of the claimed genus of methods of treating a "retinal or choroidal degenerative diseases or conditions associated with increased expression of MT1-MMP".

The instant claims are drawn to a method of treating a "retinal or choroidal degenerative disease or condition associated with increased expression of MT1-MMP" with an antibody specific for MT1-MMP. However, MMPs such as MT1-MMP are broadly expressed in tissues of the eye under various conditions of health and disease. Furthermore, the instant claims do not specify what degree of "increase" of MT1-MMP expression is required, or what the "increase" is to be compared to. For example, the claims might encompass treating conditions where the expression of MT1-MMP is "increased" in the retina relative to other parts of the eye (as is the case in the normal eye, see Smine et al.). Given the broad expression of MT1-MMP, and the lack of claim limitations regarding the "increased" expression, the instant claims might encompass treating a wide range of different conditions characterized by different etiologies and pathological mechanisms. For example, the claims might encompass treating AMD, glaucoma, retinal detachment, choroidal neoplasms, retinal or choroidal injuries or infections, etc. In contrast to the broad genus of diseases and conditions encompassed by the claims, the specification only discloses a single species of disease associated with increased expression of MT1-MMP, AMD. Thus, one of skill in the art would conclude that the specification fails to provide adequate written description to demonstrate that Applicant was in possession of the claimed invention. See *Eli Lilly*, 119 F. 3d 1559, 43, USPQ2d 1398.

10. Claims 1-2, 4-13, 15-17, 53, 57-58, and 60 are rejected

Art Unit: 1644

under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method for treating a subject having age related macular degeneration with an antibody that specifically binds MT1-MMP and decreases the activity of MT1-MMP protein, does not reasonably provide enablement for:

a method for treating a subject having or at risk of developing a retinal or choroidal degenerative disease or condition with an antibody that decreases the expression of MT1-MMP gene or protein, or an agent that decreases the activity of MT1-MMP protein.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable.

The specification provides insufficient guidance to enable claims drawn to the method as broadly claimed. The instant claims encompass treating any retinal or choroidal degenerative condition associated with increased expression MT1-MMP, with any agent that inhibits the expression or activity of MT1-MMP.

Art Unit: 1644

However, MMPs such as MT1-MMP are broadly expressed in tissues of the eye under various conditions of health and disease, and impact nearly every aspect of eye physiology (see Sivak et al. and Smine et al.). For example, MMPs, including MT1-MMP are upregulated in response to inflammation, tissue injury, or neovascularization and play a role in regenerative and healing processes. Thus, the instant claims might encompass treating diseases or conditions with widely different pathological mechanisms, including eye injuries, infection of the eye, choroidal cancer, glaucoma, and AMD. It is unlikely that a single treatment would be effective for such a diverse set of conditions. Furthermore, it is known that while MMPs in general represent an attractive therapeutic target in many retinal diseases, the effect of MMP inhibitors in particular retinal disease is still unpredictable. For example, in some instances inhibition of MMPs might inhibit routine matrix remodeling and upkeep, leading to adverse effects on the eye (see Sivak et al., page 9 in particular). Additionally, the instant claims encompass not only treating established retinal disease, but treating subjects at risk of developing said diseases by diagnosing a subject as being at risk of developing a disease or condition. This would require being able to determine which subset of normal subjects would be likely to develop virtually any retinal or choroidal condition or diseases having a wide range of etiologies, including those caused by injury or infection. It is unclear how it would be possible to diagnose a risk of developing retinal choroidal diseases associated with factors such as injury or infection, as is encompassed by the claims. Furthermore, the instant method comprises treating retinal or choroidal diseases with an antibody that decreases the expression of MT1-MMP gene or protein. While antibodies are well known therapeutic agents for inhibiting the activity of proteins *in vivo*, little is known about the ability of antibodies to inhibit gene expression.

Thus, based on the state of the art, the instant specification must provide a sufficient and enabling disclosure commensurate in scope with the instant claims. The instant specification demonstrates that MT1-MMP expression is associated with AMD, and that administration of an MT1-MMP antibody is effective in treating an animal model of AMD. However, no evidence is provided that antibodies specific for MT1-MMP are effective for decreasing the expression of MT1-MMP gene, or that said antibodies are effective for treating the broad range of other retinal or choroidal conditions encompassed by the claims.

Art Unit: 1644

Therefore, based on the unpredictability of the art and the lack of guidance provided by the instant specification, it would require undue experimentation to practice the full scope of the claimed method.

11. Claims 1-2, 4-13, 15-17, 53, 57-58, and 60 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) A method of treating a "mammalian subject" with an agent that decreases the expression or activity of MT1-MMP (Claim 1, and dependant claims 2, 4-17, 53, 57-58, and 60).

B) A method of treating a retinal or choroidal degenerative disease or condition "that is associated with increased expression of MT1-MMP" (Claim 1 and dependent claims 2, 4-17, 53, 57-58, and 60).

Applicant has not cited any support for the new limitation in the specification. A review of the specification fails to reveal support for the new limitations.

Regarding A), at page 53, the specification discloses administering a nucleic acid composition to a mammalian subject. However, the specification does not disclose treating retinal or choroidal diseases in a mammalian subject with an agent that decreases the expression or activity of MT1-MMP, as claimed.

Regarding B), at page 10, the specification discloses treating retinal or choroidal degenerative diseases or conditions, but does not disclose treating the subgenus of retinal or choroidal degenerative diseases "associated with increased expression of MT1-MMP", as now claimed.

12. No claim is allowed.

Art Unit: 1644

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 8am - 5pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Amy E. Juedes, Ph.D.
Patent Examiner
Technology Center 1600


1304
G.R. EWOLDT, PH.D.
PRIMARY EXAMINER